# STEREOSELECTIVE REDUCTIONS OF THE SOME METHYL KETONES FROM BICYCLO[2,2,1]HEPTANE AND BICYCLO[2,2,2]OCTANE SYSTEM

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**Abstract:** In the reactions of racemic *endo*-2-acetyl-bicyclo[2,2,1]heptene (I), *endo*-2-acetyl-bicyclo[2,2,1]heptane (IV) and *endo*-2-acetyl-bicyclo[2,2,2]octane (V), with the many of variety reducing agents, *endo*-α-methyl-2-methanols with the 2S, αR or 2R, αS configuration (II) were always formed in excess over the corresponding diastereomeric *endo*-alcohol (III) with the 2S, αS or 2R, αR configuration. In these nucleophilic additions stereoselectivity was low for the reducing agents $NaBH_4$ and $LiAlH_4$ but increased when the reducing reagents with bulky groups were used, *i.e.* $R_3BH$, $B_2H_6$ and $R_3AlH$. Steric control of these 1,2-asymetric reduction is discussed in terms of the open-chain transition models of the Cram and Karbatsos type.

## Introduction

The open-chain model for the Cram rule of steric control of 1,2-asymmetric induction has been successfully applied in many cases for the qualitative interpretation and predication of the preferred stereochemical course of the kinetically controlled reactions of the chiral ketones, with different the complex metal hydride and other reducing reagents [1,3].

According to this rule (the Cram`s rule), the predominating steroisomer will be that one which would be formed by the approach of entering group from the less hindered side of the

carbonyl double bond. The minor diastereoisomer would be formed by attack from the more hindered side or from an other transition state conformations. In the application of the open-chain model (and the other models as well [2,3]) the major problem is the ordering of the groups at the α-hiral center with respect to their effective size (*i.e.* L=large, M=medium, S=small). When hydrogen is present (at the α-asymmetric carbon atom) it is always the smallest group (S) while for other simple saturated groups (as substituents attached to the α-carbon atom) the relative size (bulk) order usually follows the Chan-Ingold-Prelog sequence rule [4,5].

However, when more complicated structures are involved (as substrates), the sequence rule to determine the effective size of the substituted groups can not be applied, and as this case must be considered and analyzed separately.

## Experimental

IR spectra were recorded neat are in $CCl_4$ solution on Perkin Elmer Grating Spectrophotometer Model 137 and Model 197. NMR spectra were recorded on Varian Spectrometer Models A-60, FT-80 and Gemini 200 in $CDCl_3$ solution and TMS as internal standard were used, chemical shifts are given in δ (ppm), coupling constants J in Hz. Abbrevations for designating hydrogens: x-exo, n-endo, s-sin and a-anti. For fractional destillations were used semi-micro Vigreux columns. Gas-chromatography Varian Aerograph instruments series 3400 FID) for analytical purpose, Perkin Elmer model 3920 (FID) for analytical purpose, Varian Aerograph instruments Model 940 (TSD) and Perkin Elmer F-33(TSD) for preparative separations, the columns: 15% TCEP (4 m,1/8``), 20% Carbowox 20M (4 m, 1/8``), 5% xe 60 (2 m, 1/8``) an Chromosorb P or W were used.

### Synthesis endo and exo acetylbicyclo[2,2,1]hept-5-ene (I and Ix)

A mixture of endo-2-acetyl-5-norbornene [18] (I) and its exo-isomer (Ix) b.p. 358-362 K/24 mB was obtained (about 86% yield) from cyclopentadiene and methyl-vinil ketone according to the Diels-Alder procedure. The two stereoisomers (I) and (Ix) were separeted and isolated by preparative GC on Carbowox 20M. The endo-ketone had longer retention time (yield 81%, purity 99,5%). Spectral data according to the literature [10-14].

### Synthesis endo and exo acetylbicyclo[2,2,2]oct-5-ene (V and Va)

A mixture of the endo 2-acetyl-bicyclo[2,2,2]oct-5-ene (V) and exo isomer (Va) b.p. 375 K/26 mB was obtained (in about 60% yield) from 1,3-cyclohexadiene and methyl-vinyl ketone according to the Diels-Alder procedure. The two stereoisomers (exo:endo=10:90) were separated and isolated by preparative GC on Carbowox 20M. Whereby the endo-ketone had longer retention time (yield 56%, purity 99,5%). Spectral data according to the literature [10-14].

### Synthesis endo 2-acetylbicyclo[2,2,1]heptane (IV)

The ketone (I) was hydrogenated on the atmospheric pressure during 2 hours in the presence catalytic amounts of the 10% Pd/C (yield 96%, purity 99,5%). Spectral data according to the literature [14].

### Typical Procedure for the reductions [16]

a. A mixture of 0.023 g ($6 \times 10^{-4}$ mol) $LiAlH_4$ in 10 mL was refluxed during 10 min. After adding 0.082 g ($6 \times 10^{-4}$ mol) ketone the reaction mixture was refluxed 2 h, then cooled and hydrolyzed with water and 10% $H_2SO_4$. After drying and evaporation the crude reaction mixture was analyzed (Table I). The reaction procedure in THF was identical.

b. A sufficient quantity of $LiAlH_4$ in THF to provide 0.07 mmol of hydride was placed in the reaction vessel. The solution was cooled to -5°C and 0.20 mmol of ter-butyl alcohol was slowly added as the hydrogen was vented. Ketone (0.75 mmol) was added at rates to maintain the temperature at -5°C. After stirring at room temperature during 2 hours, the reaction mixture was cooled and hydrolyzed with 10% $H_2SO_4$. The crude reaction mixture was analyzed (Table I). The reaction procedure in ether was identical.

c. A sufficient quantity of $NaBH_4$ in methanol to provide 0.07 mmol of hydride was placed in the reaction vessel. The ketone (0.07 mmol) was added during 15 min., and after stirring at room temperature during 2 hours, the reaction mixture was cooled and hydrolyzed with 5% HCl. The

crude reaction mixture was analyzed (Table I). The reaction procedure with KBH₄ and LiBH₄ were identical.

**d.** A trace of methyl orange was dissolved in water (0.1 mL) and added to THF (2 mL). Then ketone (0.07 mmol), NaCNBH₃ (0.07 mmol) and solution of HCl/AcOH in THF were added in dropwise with stirring to maintain the red color. After 5 min. the red color was persists. Stirring was continued for 2 hours. The solution was poured into water (100 mL), saturated with NaCl and extracted with ether (3x10 mL). The combined extracts were dried and evaporated in vacuo. The crude reaction mixture was analyzed (Table I).

**e.** A solution of (0.05 mmol) AlCl₃ in 50 mL of ether was prepared in ice-bath. To this solution of LiAlH₄ (0.013 mmol) in 15 mL of ether with stirring was added. The ketone (0.05 mmol) in 50 mL ether was added slowly and after this mixture refluxed during 2 hours addition was complete. The reaction mixture was hydrolyzed with 10% (NH₄)₂SO₄ and the crude products were analyzed (Table I). The reaction procedure in THF was identical.

**f.** A sufficient quantity of NaBH₄ (2 mmol) and of the ketone (2 mmol) was added to BF₃·Et₂O (2.5 mmol, 3M solution in diglim). After standing at 25°C for 3 hours, the reaction mixture was heated at 40-45°C for 3 hours. The excess of hydride was destroyed with 2M HCl. The crude product was analyzed (Table I).

**g.** To suspension of sodium (powder, 0.09 mmol) in benzene (50 mL), ketone (60 mmol) in the mixture of *iso*-propanole (7 mL) and benzene (20 mL) was added. This solution was added during 30 min. The mixture was refluxed for 2 hours. The excess of Na was destroyed with *iso*-propanole. After hydrolysis with water, benzene layer was washed with water, dried and evaporated. The crude product was analyzed (Table I).

**h.** A sufficient quantity of diisobutylaluminium hydride (DIBAL) in toluene to provide 0.07 mmol of hydride was placed in the reaction vessel. The solution was cooled to -5°C. The ketone was added at a rate as to maintain temperature at 0°C. After stirring at 0°C during 2 hours the mixture was hydrolysed and the crude products were analyzed (Table I).

**i.** The ketone was hydrogenated with hydrogen on the atmospheric pressure during one hour in the presence of PtO₂ in ethanol. After separation and isolation the crude reaction product was analyzed (Table I).

*Spectral data for products*

*endo*-α-**methylbicyclo[2,2,1]hept-5-en-2-methanol**, (diastereoisomer II, 2R, αS or 2S, αR), colorless oil, $n_d^{20}$ 1.4913 shorter $t_r$; IR: $v_{max}$ (cm⁻¹) 3360, 3070, 1560, 1090, 720. NMR 1.08 (CH₃, J=6), 1.25-1.41 (C₇ₐ-H and C₇ₛ-H), 1.5-2.2 (C₂ₓ-H and C₃ₓ-H), 2.75 (C₄-H), 3.16 (Hₐ, J=9), 3.06 (C₁-H), 6.08 (C₅-H and C₆-H), 0.4-0.52 (C₃ₙ-H). MS parent ion C₉H₁₄O, m/z=138.105, base peak (retro Diels-Alder), C₅H₆ m/z=66, m/z=123; (M⁺-15), 120 (M⁺-18), 105(M⁺-15-18), 91.

*endo*-α-**methylbicyclo[2,2,1]hept-5-en-2-methanol**, (diastereoisomer III, 2S, αS or 2R, αR), m.p.=34-35°C, $n_d^{20}$ 1.4913 longer $t_r$; IR: $v_{max}$ (cm⁻¹) 3270, 3070, 1567, 1104, 730. NMR 0.91 (C₃ₙ-H), 1.15 (CH₃, J=6), 1.2-1.5 (C₇ₐ-H and C₇-H), 1.5-2.1 (C₂ₓ-H and C₃ₓ-H), 2.8 (C₁-H), 3.19 (H, J=7), 5.9 (C₅-H), 6.1 (C₆-H, J=4). MS parent ion C₉H₁₄O, m/z=138.105, base peak C₄H₉, m/z=66,(retro Diels-Alder), m/z=123, (M⁺-15), 120 (M⁺-18), 105(M⁺-15-18), 93 (M⁺-43).

*endo*-α-**methylbicyclo[2,2,1]hept-5-en-2-methanol**, (diastereoisomer VII, 2S, αR or 2R, αS), m.p.=36-38, shorter $t_r$ $n_d^{20}$ 1.4913; IR: $v_{max}$ (cm⁻¹) 3320, 1370, 1098, 896. NMR 0.53 (C₃ₙ-H), 1.15

(CH$_3$), 2.2 (C$_4$-H), 3.65 (C$\alpha$-H), 2.35 (C$_1$-H). MS m/z=140 (M$^+$), 122 (M$^+$-18, 100%), 107(M$^+$-15-18), 95(M$^+$-45), 66 (retro Diels-Alder).

*endo*-$\alpha$-methylbicyclo[2,2,1]hept-5-en-2-methanol, (diastereoisomer VIII, 2S, $\alpha$S or 2R, $\alpha$R), colorless oil, n$_d^{20}$ 1.4834, longer t$_r$; IR: v$_{max}$ (cm$^{-1}$) 3360, 1370, 1120,1070, 745. NMR 0.95 (C$_{3n}$-H), 2.13 (C$_1$-H), 2.21 (C$_4$-H), 3.54 (C$\alpha$-H),), 1.19 (CH$_3$). MS m/z=140 (M$^+$), 122 (M$^+$-18, 100%), 107(M$^+$-15-18), 95(M$^+$-43), base peak C$_7$H$_{11}$.

*endo*-a-methyl-bicyclo[2,2,1]hept-5-en-2-methanol, (diastereoisomer IX and X, mixture 2S, $\alpha$R or 2R, $\alpha$S and 2S, $\alpha$S or 2R, $\alpha$R ), IR: v$_{max}$ (cm$^{-1}$) 3350, 3070, 1470, 1380, 1070, 705. NMR 6.25 (C$_5$-H,C$_6$-H), 3.32 (C$\alpha$-H),), 1.03 (CH$_3$, J=6) and 1.08 (CH$_3$, J=6). MS m/z=152 (M$^+$), 134 (M$^+$-18), 119(M$^+$-15-18), 107(M$^+$-43), 80 (retro Diels-Alder).

**(2R,3S or 2S,3R)-2-methylhexahydro-3,5-methano-2H-cyclo-penta[b]furan** ( diastereo-isomer XI, H$_2$/H$_3$ *trans*) colorless liquid, n$_d^{20}$ 1.4751, shorter t$_r$; IR: v$_{max}$ (cm$^{-1}$) 1380, 1142,1089, 1075, 1042, 1013. NMR 4.32 (C$_{6-exo}$-H), 2.71 (C$_1$-H), 3.91 (C$\alpha$-H),), 1.04 (CH$_3$, J=6.2). MS m/z=138 (M$^+$), 123 (M$^+$-15), base peak C$_8$H$_{11}$O.

**(2R,3R or 2S,3S)-2-methylhexahydro-3,5-methano-2H-cyclo-penta[b]furan** ( diastereo-isomer XII, H$_2$/H$_3$ *cis*) colorless liquid, n$_d^{20}$ 1.4772, longer t$_r$; IR: v$_{max}$ (cm$^{-1}$) 1388, 1151,1131, 1098, 1080. NMR 4.15 (C$_{6-exo}$-H), 2.70 (C$_1$-H), 3.92 (C$_\alpha$-H),), 1.12 (CH$_3$, J=6.3). MS m/z=138 (M$^+$), 123 (M$^+$-15), 105 (C$_8$H$_{11}$O).

**(2R,3S or 2S,3R)-6-exo-bromo-2-methylhexahydro-3,5-methano-2H-cyclo-penta[b]furan** ( diastereoisomer XIII, H$_2$/H$_3$ *trans*) colorless oil. IR: v$_{max}$ (cm$^{-1}$) 1450, 1378,1150, 1040, 845,790, 760. NMR 4.46 (C$_{6-exo}$-H, b d,J=5), 3.92 (C$_2$-H,q, J=6.5), 3.58 (C$_{6-endo}$-H, d, J=2.5) 2.75 (C$_{3\beta}$-H, m), 1.04 (CH$_3$, J=7). MS m/z=218 (M$^{+81}$), 216 (M$^{+79}$), 203 (218-15), 201 (216-15), 137 i 135 (218-HBr), 93, 43.

**(2S,3S or 2R,3R)-6-exo-bromo-2-methylhexahydro-3,5-methano-2H-cyclo-penta[b]furan** ( diastereoisomer XIV, H$_2$/H$_3$ *cis*) colorless oil. IR: v$_{max}$ (cm$^{-1}$) 1440, 1380,1180, 1160,1065, 1025, 940, 840, 790, 760. NMR 4.30 (C$_{6-exo}$-H, b d,J=5), 3.95 (C$_2$-H, d q, J=3), 3.52 (C$_{6-endo}$-H, d, J=2) 2.75 (C$_{3_\alpha}$-H, m), 1.12 (CH$_3$, d, J=7). MS m/z=218 (M$^{+81}$), 216 (M$^{+79}$), 203 (218-15), 201 (216-15), 137 i 135 (218-HBr), 119 (201-HBr)93, 43.

**(2S,3R or 2R,3S)-6-exo-hydroxy-2-methylhexahydro-3,5-methano-2H-cyclo-penta[b] furan** ( diastereoisomer XV, H$_2$/H$_3$ *trans*) colorless oil. IR: v$_{max}$ (cm$^{-1}$) 3400, 2940, 2860,1370, 1145, 1020. NMR 3.8-4.2 (C$_{6\alpha-exo}$-H and C$_2$-H, m), 3.42 (C$_{6-endo}$-H, b s) 2.72 (C$_{3_\alpha}$-H, m), 1.07 (CH$_3$, J=7). MS m/z=154 (M$^+$), 139 (154-15), 136 (154-18), 123(154-31), 83 (C$_5$H$_7$).

**(2S,3S or 2R,3R)-6-exo-hydroxy-2-methylhexahydro-3,5-methano-2H-cyclo-penta[b] furan** ( diastereoisomer XVI, H$_2$/H$_3$ *cis*) colorless oil. IR: v$_{max}$ (cm$^{-1}$) 3380, 2960, 1340, 1100, 1040. NMR 3.8-4.2 (C$_{6\alpha-exo}$-H and C$_2$-H, m containing a broad d, J=5), 3.40 (C$_6$-H and C$_{11}$-H formed d, J=2) 2.70 (C$_{3_\alpha}$-H, m), 1.21 (CH$_3$, J=6.5). MS m/z=154 (M$^+$), 139 (154-15), 136 (154-18), 123(154-31), 83 (C$_5$H$_7$), 66, 55.

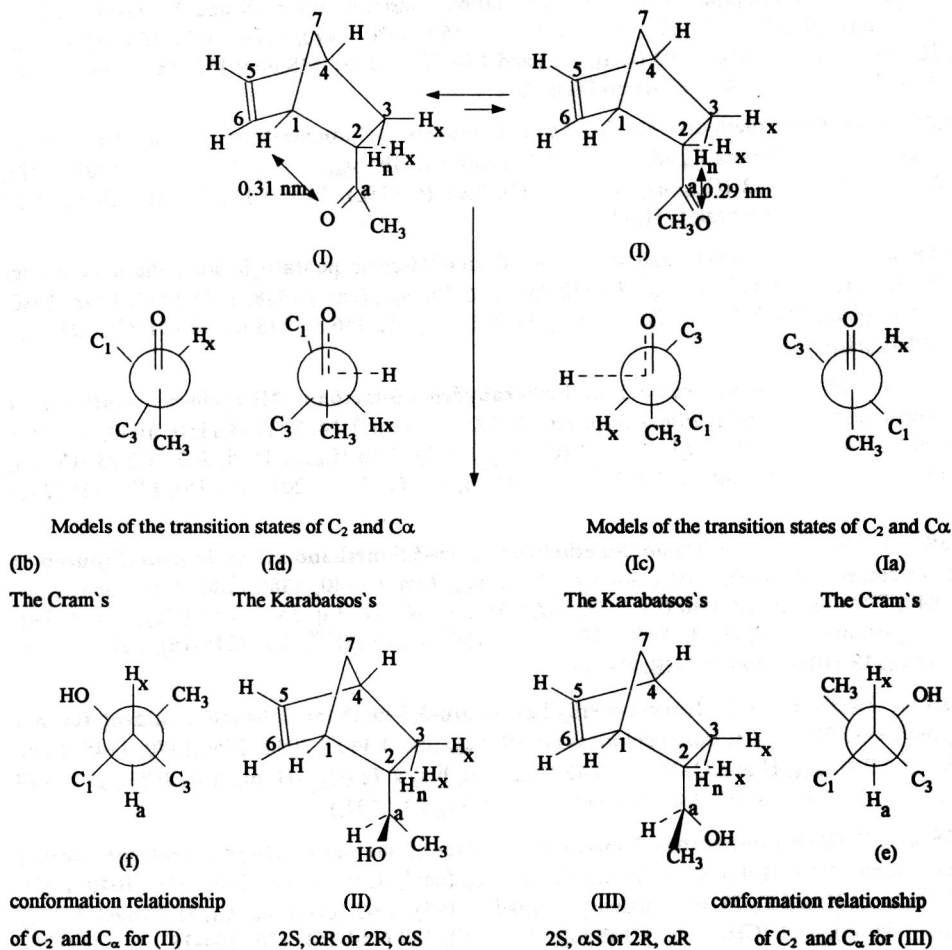## Results and discussion

Such example are the *endo*-2-acetyl-derivatives of the bicyclo[2,2,1]heptene, bicyclo[2,2,1]heptane and bicyclo[2,2,2]octene series, which was used, in the present study, as substrate for investigating the extent of 1,2-asymmetric induction in the reactions with the some reducing reagents, (*i.e.* the stereoselectivic conversion *endo*-2-acetyl-5-norbornene (I) to the

diasteremetric *endo* α-methyl-5-norbornene-2-methanols (II and III) [11-13]. The results obtained for all substrates in the bicyclo[2,2,1]heptene, bicyclo[2,2,1]heptane and bicyclo[2,2,2]octene series are presented in the Table I.

*Cram-type models*

In the case of *endo*-ketone (I) the α-asymmetric carbon atom, $C_2$ is attached to $C_{2-exo}$, $C_3HHC$ and $C_1HCC$ (Scheme 1).



Models of the transition states of $C_2$ and $C\alpha$          Models of the transition states of $C_2$ and $C\alpha$

(Ib)                    (Id)                              (Ic)                    (Ia)

The Cram's              The Karabatsos's                  The Karabatsos's        The Cram's

(f)                     (II)                              (III)                   (e)

conformation relationship    2S, αR or 2R, αS             2S, αS or 2R, αR        conformation relationship

of $C_2$ and $C_\alpha$ for (II)                                                  of $C_2$ and $C_\alpha$ for (III)

Scheme 1.

According to the Chan-Ingold-Prelog sequence rule the order of increasing priority is $H_2 < C_3 < C_1$. If this would also represent the size group order, then the favoured open-chain transition state model for the additional reducing reagents would be conformation (Ia) (Scheme 1) and the diastereimetric alcohols (III) should be formed in excess.

On the other hand, from inspection of molecular models, constructed according to literature values for bond angles, dihedral angles and bond lengths [5-7], it appears that conformation (Ib) for the transition state model is somewhat more stable than conformation (Ia) (*i.e.* that $C_3$ acts as large (L) and $C_1$ as medium (M) group since in this conformation (Ib) the distance $O-H_{(C1)}$ (about 0.31 nm) is slightly greater than the distance $O-H_{(C3-endo)}$ (about 0.29 nm) in conformation (Ia) and that therefore the reducing reactions be mainly controlled by (Ib) and should afford as major diastereoisomer alcohol (II) (Scheme 1).

*Karabatsos-type model* [8,9]

It is also possible and perhaps even more convenient, to consider as model the transition state configurations corresponding to ketone (I) with eclipsed carbonyl and steggered methyl group as in the Karabatsos semi empirical treatment of steric control of 1,2 asymmetric induction [2,3,6], in that case according to molecular models and taking the same size order of groups as above $H_{2-exo} < C_1 < C_3$, among conformation in which approach of the nucleophile is sterically least hindered and these are two conformations (Ic) and (Id) show in the Scheme 1. The conformation (Vd) leading to the diastereoisomer (II) appears to be somewhat more stable than conformation (Ic) which affords the diasteremeric alcohol (III), this is in agreement with the preferential formation of the diastereoisomer (II) from the ketone (I) and the different reducing reagents (Table I).

Table I. Steroselectivity in the conversion of *endo*-2-acetylbicyclo[2,2,1]hept-5-ene (I), *endo*-2-acetylbicyclo[2,2,1]heptane (IV) and *endo*-2-acetylbicyclo[2,2,2]oct-5-ene (V), to the corresponding diastereoisomeric alcohols

| Run | Reducing reagents | Ratio and Stereoselectivity in % [17] | | |
| --- | --- | --- | --- | --- |
| | | a:b, (I) | a:b, (IV) | a:b, (V) |
| 1. | LiAlH$_4$, Et$_2$O | 51:49, (2) | 70:30, (40) | 57:43 (14) |
| 2. | LiAlH$_4$, THF | 57:43, (14) | 76:24, (52) | 55:45, (10) |
| 3. | ($t$-C$_4$H$_9$O)$_3$LiAlH, Et$_2$O | 58:48, (16) | 75:25, (50) | 58:42, (16) |
| 4. | ($t$-C$_4$H$_9$O)$_3$LiAlH, THF | 65:35, (30) | 81:19, (62) | 61:39, (22) |
| 5. | NaBH$_4$, MeOH | 58:48, (16) | 63:37, (26) | 55:45 (10) |
| 6. | KBH$_4$, MeOH | 55:45, (10) | - | - |
| 7. | LiBH$_4$, MeOH | 52:48, (4) | 57:43, (14) | 53:47 (6) |
| 8. | NaCNBH$_3$, MeOH | 51:499, (2) | - | - |
| 9. | AlCl$_2$H, Et$_2$O | 72:28, (44) | 79:21, (58) | 70:30 (40) |
| 10. | AlCl$_2$H, THF | 74:26, (48) | 89:11, (78) | 72:28 (44) |
| 11. | DIBAL | 62:38, (24) | 85:15, (70) | 61:39 (22) |
| 12. | B$_2$H$_6$, diglim | 77:23 (54) | - | - |
| 13. | Na, *iso* C$_3$H$_7$OH | 35:65, (30) | 40:60, (20) | 41:39 (22) |
| 14. | H$_2$ / PtO$_2$ | 90:10, (80) | 94:6, (88) | 86:16 (72) |

**Conclusion**

Table I shows the ratios of the diasteremeric alcohols (a:b) obtained (in yield 70-85%) in the reactions reductions corresponding *endo*-2-acetyl derivatives with the different reducing agents. It can be seen:

1. Alcohols (II and VII) were always formed in excess to their diastereisomers (III and VIII).

2. The stereoselectivity was low when LiAlH$_4$ and NaBH$_4$ were used as reducing reagents but, as expected, increased with increasing steric bulk of the reducing agents *i.e.* when progressing from LiAlH$_4$, (*t*-C$_4$H$_9$O)$_3$AlH to AlCl$_2$H. From these results it appears that conformation (Ib) in the Cram-type model should be used for interpreting and/or predicting the stereochemical outcome of the reducing reagents addition reactions performed with the *endo*-ketones.

## Assignement of configuration

The relative configuration of the diastereomeric α-methyl substituted alcohols (II and III) [11,13] were determined previously by first order analysis of their $^1$H NMR spectra and by conversion to the cyclic ether products [10,14].

On the basis the coupling between H$_\alpha$ and H$_{2x}$ ($^3$J=9-7 Hz) in compounds (II and III), and compared with axial-axial coupling observed in the rigid cyclohexanoic system in which one carbon involved bears an oxigen substituent, it was indicated that alcohols (II and III) exist predominantly in the conformations in which the spatial orientation of H$_\alpha$ and H$_{2x}$ is very close to the *anti*-arrangement (Scheme 1). It should be noted that these conformers are also favoured for steric aspect.

Such different geometrical relationships of the substituents (OH, CH$_3$) at C$_\alpha$ with respect to the bicyclic system in two diastereomeric alcohols, having conformation (II and III) respectively, should result in different anisotropic effect due to the hydroxyl and methyl groups. This could than possibly explain the large downfield shift (0.5 ppm) of the H$_{3n}$ signal in the alcohol (III) from usual position this proton in the alcohol (II) [15]. Actually the H$_{3n}$ signal of the alcohol (II) appears to be slightly displaced to downfield, possibly because of the 1,3 influence of the methyl group.



(II) 2R, αS or 2S, αR                         *trans*

(III) 2S, αS or 2R, αR                         *cis*
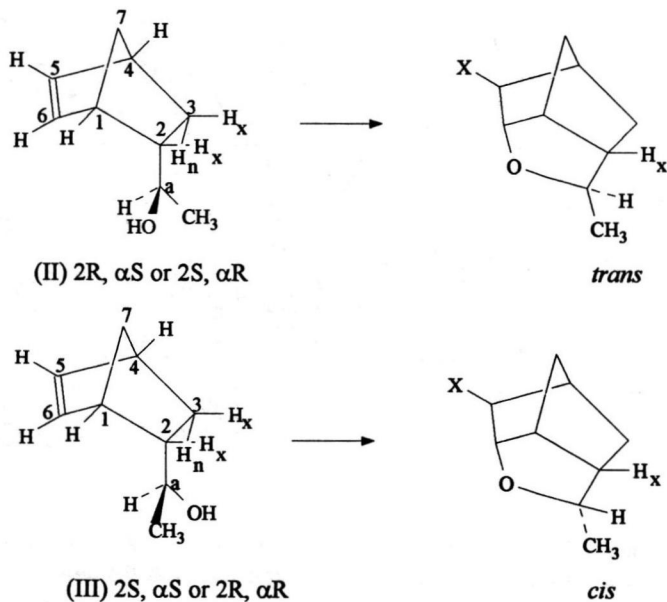
Scheme 2.

The same explanation could account for the smaller downfield displacement of the protons $H_1$ and $H_6$ signals in the alcohol (II, 0.2 and 0.15 ppm). If these effects are due as expected to the influence of the hydroxyl group rather than the methyl group, in this way, the signals for the two olefinic protons $H_5$ and $H_6$ are equivalent and situated at about 6.1 ppm ($J_{\omega/2}$=4.5 Hz). The alcohol (II) would have the stereochemistry of conformer (f) *i.e.* the 2S, $\alpha$R or 2R, $\alpha$S configuration. In the case for the other alcohol (III), the signals for two olefinic protons are separated from one to another (by about 0.2-0.3 ppm) the $H_5$ signal is located at about 6.1 ppm and the $H_6$ signal at about 5.8 ppm. The alcohol (III) would have conformer (e) *i.e.* the 2S, $\alpha$S or 2R, $\alpha$R configuration.

The structure and stereochemistry of alcohols (II and III) also were determinated through formation of the corresponding cyclic ethers and their derivatives [10-14]. When the diastereomeric pairs of the *endo*-$\alpha$-methylbicyclo[2,2,1]hept-5-en-2-methanol(2R, $\alpha$S; 2S, $\alpha$R or 2S, $\alpha$S; 2R, $\alpha$R) are subjected to the acid catalysis, the oxymercuration-demercuration reaction, the reaction with peracids and the raection with NBS [14] they undergo due to neighboring group participation, intramolecular ether ring clousure in a regioselective way, affording exclusively corresponding the two epimeric 3-methyl-2-oxatricyclo[4,2,1,0$^{4,8}$]nonanes [19].

The structure and stereochemistry of the ethers and their bromo and hydroxy derivatives were deduced from the $^1$H NMR spectra (by analysing the position multiplically and splitting constants of the relevant signals) by comparison with the spectra of the starting alcohol (II and III).

Thus, in the spectrum of the cyclic ether (XI) obtained from alcohol (II), the coupling between $H_\alpha$ and $H_{2x}$ ($^3$J=0.0 Hz, $\tau$=78$^0$C) corresponds to the *trans*- $H_\alpha$ and $H_{2x}$ arrangement, whereas in the spectrum of the epimeric cyclic ether (XII) derived from alcohol (III), this coupling ($^3$J=3.6 Hz, $\tau$=48$^0$C) is in accordance with the *cis*- $H_\alpha$ and $H_{2x}$ geometry (Scheme 2).

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[17] In runs 1-11 and 13 the ratio of the stereoisomers was calculated from gas chromatograms, whereas in runs 12 and 14 this ratio was estimated from NMR spectra.

[18] * 2-acetyl-bicyclo[2,2,1]hept-5-ene.

[19] Naming of the tricyclic ether products (nomenclature):

CHEM.ABSTR.: 2-methylhexahydro-3,5-methano-2H-cyclopenta[b]furan

IUPAC: 3-methyl-2-oxatricyclo[4,2,1,0$^{4,8}$]nonane.

## STEROSELEKTIVNOST REDUKCIJA *ENDO*-METIL KETONA BICIKLO[2,2,1]HEPTANSKE I BICIKLO[2,2,2]OKTANSKE SERIJE

### S. Sukdolak, S. Solujić G. Stojanović

U reakcijama redukcije *endo*-metil ketona biciklo[2,2,1]heptanske i biciklo[2,2,2]oktanske serije sa različitim redukcionim agensima dobiveni su odgovarajući stereoizomerni *endo*-α metil-2-metanoli. Konformer 2S, αR ili 2R, αS je dobiven uvek u višku u odnosu na 2S, αS ili 2R, αR konformer. Sterna kontrola ovih 1,2-asimetričnih redukcija je diskutovana i tumačena primenom Cram-ovog i Karabatsos-ovog pravila.